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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/808,878 | 03/15/2001 | James H. Pickar | AM100226 | 5270 |

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| EXAMINER | |
|---|---|
| BAHAR, MOJDEH | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | 18 |

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application N . | Applicant(s) | |
|---|---|---|---|
| | 09/808,878 | PICKAR, JAMES H. | |
| | Examin r | Art Unit | |
| | Mojdeh Bahar | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**P riod for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7,11,12 and 15-69* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 15-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,11,12 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15,17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Applicant's response filed April 7, 2003 and the declaration submitted under 37 CFR 1.132 with attached references are acknowledged.

This application contains claims 1-6 and 15-68 drawn to an invention nonelected with traverse in Paper No. 5. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 7, 11, 12 and 69 are examined herein in so far as they read on the elected specie of hot flashes.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7, 11, 12 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Plunkett et al. (USPN RE 36,247).

Plunkett et al. (USPN RE 36,247) teaches a method of treating hot flashes comprising administering continuously and uninterruptedly both progestogen and estrogen in daily dosage units, see claims 21-34, col. 3, lines 51-59 and col.8 lines 62-64 in particular. Plunkett et al. (USPN RE 36,247) also teaches conjugated equine estrogen/medroxyprogesterone as one of the estrogen/progestogen combinations useful in its method, see claims 21-34. Plunkett teaches the minimum and maximum dosages for medroxyprogesterone and conjugated equine estrogens to

be 1 mg/day and 15 mg/day and 0.300 and 2.5 mg/day (preferred dosage of 0.300-0.600 mg) respectively, see claims 34-35, see also Table 1A, col.4, in particular.

Plunkett et al. does not particularly teach the dosages of conjugated equine estrogen/medroxyprogesterone claimed herein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ conjugated equine estrogen/medroxyprogesterone in the specific dosages claimed herein in a method of treating hot flashes.

One of ordinary skill in the art would have been motivated to employ conjugated equine estrogen/medroxyprogesterone in the specific dosages claimed herein in a method of treating hot flashes because they (dosages herein) fall within the therapeutic ranges of the conjugated equine estrogen/medroxyprogesterone taught by the prior art. Optimization of amounts is within the purview of the Skilled Artisan, and is therefore obvious absent evidence to the contrary. No such evidence is seen.

***Response to Arguments***

Applicant's arguments filed April 7, 2003 have been fully considered but they are not persuasive. Applicant first argues that "there is nothing in Plunkett to teach or suggest the selection of 1.5 mg MPA for the treatment of vasomotor symptoms in combination with about 0.3 to about 0.45 mg CEE." Note that Plunkett teaches that MPA can be employed at a minimum dosage of 1.0 mg and maximum dosage of 15 mg. Note that the claimed dosage herein, 1.5 mg, falls within the Plunkett range. Note also that the claimed dosage herein, 0.3-0.45 mg of CEE, falls within the dosage range of Plunkett, 0.300-0.600 mg, see claim 35 of Plunkett.

Applicant draws the examiner's attention to data presented in the specification showing the efficacy of the dosages herein versus that of the common daily dosages of Premarin and MPA. Note that in order to overcome obviousness applicant must demonstrate unexpected results in comparison with the closest prior art, i.e., Plunkett. No such comparative data has been provided. Applicant states that the closest example in Plunkett is a regimen comprising 0.600 mg CEE and 2.5 mg MPA. The specification on page 9 provides a comparative example between 0.625 mg of CEE, and not 0.600 mg of CEE. Furthermore the data presented does not constitute unexpected results because according to the applicant's remarks, the data shows similar efficacy of the following regimens: 0.625 CEE/2.5 MPA, 0.45 CEE/1.5 MPA, 0.30 CEE/1.5 MPA. Some data points are overlapping in both number and severity of hot flushes. Assuming *arguendo* that lower doses of MPA and CEE claimed herein yield similar therapeutic results, then the teachings of the prior art is confirmed. Plunkett teaches a wide range of CEE/MPA as effective in treating hot flushes. Therefore the showing on page 9 of the specification indeed confirms the teachings of the prior art that the entire range disclosed in Plunkett is effective in treating hot flushes.

Analyzing the data, one can observe/conclude the following:

The data provided compares 0.625 mg of CEE and 2.5 mg of MPA to 0.45 mg of CEE and 1.5 mg of MPA and 0.3 mg of CEE and 1.5 mg of MPA. Note that at 12 weeks the three regimens seem to yield comparable results, whereas at 8 weeks the higher doses of CEE yield much better results. The data presented is thus not clear because the skilled artisan cannot ascertain the efficacy of one regimen over the other. Further note that since the doses of both CEE and MPA are different in the Tables presented on page 9 (i.e., both CEE and MPA doses

are lowered simultaneously from second column to third and forth column), the additive effects of the drugs, if any cannot be ascertained.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The declaration of Dr. Lobo submitted under 37 CFR 1.132 has been carefully considered, but is not persuasive to remove the obviousness rejection herein.

First, in paragraph 7, Dr. Lobo describes the conclusion of the PEPI trial which in short concludes that the co-administration of MPA and CEE provided protection of the endometrium. Note that the prior art reference herein teaches the co-administration of MPA with CEE.

Secondly, in paragraph 8, Dr. Lobo states that in the past 20 years 0.625 mg of CEE and 2.5 mg of MPA has been recognized as the standard dosage. In support of this proposition Dr. Lobo refers to two articles, namely Lindsay et al., and Archer et al. Note that the teachings of Archer et al. are not relevant since the article was published after the filing date of the instant application. Note that a showing of unexpected results should be based on what would have been unexpected at the time of filing of an application. In regards to Lindsay et al. please note that the minimum effective dosage taught in Lindsay et al. is the minimum effective dose of estrogen in prevention of postmenopausal bone loss, Not hot flushes. Therefore this reference

does not support Dr. Lobo's proposition. Moreover, note the Plunkett et al., a patent issued in the last 20 years contradicts this very proposition since it teaches ranges of CEE/MPA that encompass the dosage claimed herein.

In paragraph 15, Dr. Lobo's declaration further states that Greendale et al. has taught no additive effect of MPA in relief of vasomotor symptoms. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the additive effect of MPA in relief of vasomotor symptoms) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Also note that there is no showing of this additive effect in the instant case. Moreover, as stated in the art, the instant combination composition is taught in the prior art. Therefore the declaration does not clearly and convincingly show unexpected benefits residing in the dosage regimen of CEE/MPA herein

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 from Monday to Friday from 9:00 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
September 16, 2002

SREENI PADMANABHAN
PRIMARY EXAMINER
9/17/03